Current PSYCHIATRY

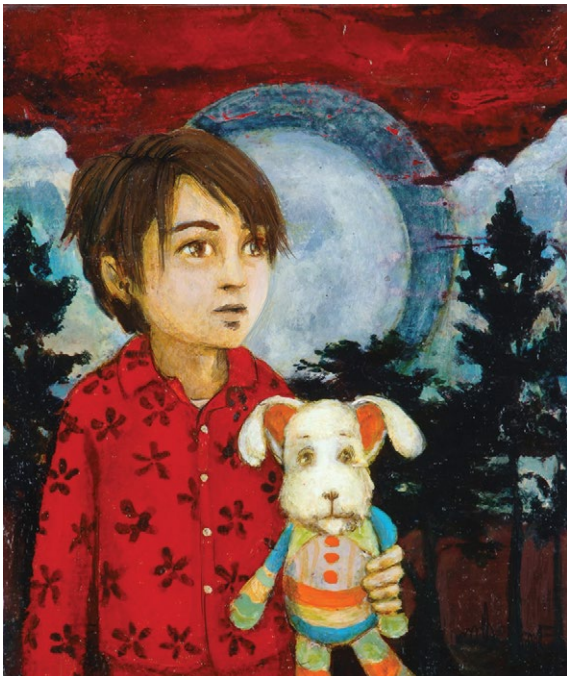
SECOND OF 2 PARTS

Pediatric insomnia: Treatment

Behavioral interventions should be implemented before considering pharmacotherapy

Children and adolescents who do not receive sufficient sleep can experience worsening inattention, daytime fatigue, and cognitive and behavioral difficulties. Assessment and treatment of insomnia and other sleep difficulties in young patients is critical as poor sleep increases their risk for depression, self-harm, and suicide.

In Part 1 of this article (Pediatric insomnia: Assessment and diagnosis, Current Psychiatry, December 2021, p. 9-13,24-25), we described sleep architecture, sleep in healthy youth and in those with certain psychiatric disorders, and how to assess sleep in pediatric patients. In Part 2, we focus on psychotherapeutic and psychopharmacologic interventions for youth with insomnia, and describe an effective approach to consultation with pediatric behavioral sleep medicine specialists.



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Psychotherapeutic interventions

Regardless of the source of a child's insomnia or co-occurring disorders, healthy sleep practices are the first line behavioral treatment, including for youth with attention-deficit/hyperactivity disorder (ADHD), anxiety disorders, obsessive-compulsive disorder, and depressive disorders.

continued

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Clinical Point

Sleep restriction should be used only after other sleep hygiene measures have been put into place for several weeks

Table

Behavioral interventions for insomnia

Sleep hygiene

1. Bedtime routine
   - Same 3 to 4 activities each night
   - Activities go in the same order each night (bath, pajamas, books, bed)
2. Bedroom environment
   - Dark
   - Quiet
   - Cool
   - Comfortable
   - Safe
   - Consistent
   - Low stimuli
3. Limit/eliminate devices in bedroom
   - Remove electronics (ie, TV, video games)
   - Limit use of handheld devices in bedroom, never in bed
   - Use a "tech check basket"—a place to hold all devices for specified period of time (ie, 10 pm to 6 am)
4. Consistent wake-up time on weekdays and weekends
   - Keep wake-up times within 1 hour on weekdays vs weekends
5. "Zeitgebers" (cues that help regulate the body's circadian rhythms)
   - Meals at consistent time on weekdays and weekends
   - Increased physical activity most days of the week
   - Exposure to daylight in the morning to set circadian rhythm for the day

Stimulus control

- Use bed for sleep only
- Other activities occur outside of bed (cellphone, computer, reading, etc)

Sleep restriction

- Possibly appropriate for adolescents when above strategies have not been successful
- Restrict sleep to 6 to 7 hours a night
- Once adolescent reaches 85% sleep efficiency or higher, add time in bed for sleep
- Do not restrict sleep any more than 6 to 7 hours for adolescents

Healthy sleep practices/sleep hygiene

Developmentally appropriate bedtimes and routines (*Table*). Helping children establish a regular, consistent bedtime is key in promoting healthy sleep. Ideally, the bedtime routine involves 3 to 4 activities each night in the same order, and these activities should be relaxing and soothing (eg, taking a bath, putting on pajamas, reading books). Setting age-appropriate bedtimes also is important. If an older child is asked to go to bed at 8 pm but cannot fall asleep for an hour, they may not have insomnia but instead a developmentally inappropriate bedtime. Several studies found that children younger than age 10 should go to bed no later than 9 pm. Bedtimes later than 9 pm for young children are correlated with shorter sleep duration.[1]

Consistent sleep schedules. Another important aspect of healthy sleep is working with parents to enforce a consistent bedtime and wake-up time, including weekdays and weekends. Ideally, bedtime on weekdays and weekends should not vary by more than 1 hour. Helping children wake up at the same time each day helps to set and regulate their circadian rhythm. Keeping these schedules consistent on vacations and school holidays also is helpful. For adolescents, the weekday/weekend bedtimes can vary by up to 2 hours because adolescents have a delayed circadian rhythm and wake-up times for high school can be early.

Environmental factors. An important piece of parental education is stimulus control and the ingredients of healthy sleep. Healthy sleep ingredients include a dark, quiet, consistent, and cool bedroom; a comfortable bed, the child feeling safe, and limited environmental stimuli.

Cognitive-behavioral therapy for insomnia

Relaxation. Pediatric patients can be taught relaxation, mindfulness, meditation, and progressive muscle relaxation techniques to help lower overall stress. This can be especially helpful for youth with sleep disorders or anxiety. Guided relaxation apps are popular among children and teens, and various apps offer soothing sounds, deep breathing, progressive muscle relaxation, and guided imagery. This can be taught in psychotherapy sessions and used at home to promote gains in between sessions.

Stimulus control. Stimulus control involves using the bed exclusively for sleep and avoiding nonsleep activities in bed (eg, reading, watching television, using a computer, worrying). These activities promote wakefulness and insomnia. This may mean the child does not get into bed until they cannot keep their eyes open, even if that delays bedtime. If the child is still awake within 15

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to 20 minutes, they should be encouraged to get out of bed and engage in a nonstimulating activity such as meditation, reading, or sitting quietly in the dark or low light. This recommendation can run counter to parents' intuition that children with sleep problems should go to bed earlier. Using the bed only for sleep conditions the child to falling asleep or being asleep when in bed.

Sleep restriction. Sleep restriction involves restricting sleep to a set number of hours in order to increase their sleep efficiency (time slept in bed divided by total time spent in bed x 100). Restricting sleep to 6 to 7 hours increases sleep efficiency, consolidates sleep, and extinguishes the association of being awake in bed. For older adolescents, sleep restriction may help to limit their time in bed to either falling asleep or being asleep. This is intended to be used as a short-term strategy and only after other sleep hygiene measures (bedtime routine, environmental factors, etc) have been put into place for several weeks. While this strategy sounds unappealing to most individuals with insomnia, it can lead to lasting change due to the use of behavioral conditioning in bed. Because sleep restriction can lead to significant daytime sleepiness and impairment during the day, sleep should not be restricted to <6 hours a day for children and adolescents. Once the adolescent is sleeping more consistently and sleep efficiency reaches 85% or higher, time in bed for sleep is increased.[2]

Cognitive restructuring. Some children and adolescents develop maladaptive thoughts about sleep that further promote insomnia. These thoughts might include "I will never get to sleep," "I am going to have a terrible day if I cannot fall asleep," or "I will fail my test tomorrow if I am unable to sleep." Such maladaptive thoughts are often untrue but promote wakefulness in the early or middle part of the night. Cognitive restructuring involves helping the child identify each problematic thought, challenge how accurate each thought is with evidence, and replace the problematic thought with a more helpful thought. For instance, an adolescent can recognize that even if they have a sleepless night, their catastrophic outcome (eg, "I will not be able to function") is likely untrue. A psychologist can help review evidence for this, including previous times when the adolescent has not slept well and managed to get through the next day.

When is pharmacologic treatment needed?

Pharmacologic treatment may be indicated if a child does not show significant improvement following behavioral intervention (***Figure, page 19***). However, it is critical to exclude other primary causes of dyssomnia (eg, obstructive sleep apnea, iron deficiency anemia) before pursuing pharmacotherapy, because pharmacotherapy could mask an underlying disorder. Moreover, while there is relatively limited evidence for psychopharmacologic interventions for sleep difficulties in children and adolescents, a large survey of child and adolescent psychiatrists (N = 1,273) suggested that medications were considered for one-quarter of pediatric patients with insomnia.[3] Further, patients with specific comorbidities such as neurodevelopmental disorders may be more likely to be prescribed soporifics.[4]

Clinical Point

Before pursuing pharmacotherapy, exclude other primary causes of dyssomnia (eg, sleep apnea, iron deficiency anemia)

What is the evidence for pharmacotherapy?

Antihistamines. Histamine antagonists—which promote sleep by blocking the wakefulness-promoting and circadian-related effects of histamine—are the most commonly used medications to treat pediatric insomnia, despite a dearth of data from prospective trials.[5,6] In 1 small study, Russo et al[7] found diphenhydramine, 1 mg/kg at bedtime, reduced sleep latency and nighttime awakenings, and increased sleep duration in patients ages 2 to 12; similar effects have been observed in pediatric burn patients.[8] There are some limited data for other H1 antagonists (eg, hydroxyzine) in pediatric insomnia.[9-11]

Alpha-2 agonists increase rapid eye movement sleep via dose-dependent downregulation of noradrenergic signaling[12] and thus have been commonly prescribed for insomnia in children and adolescents. In fact, the nonselective alpha-2 agonist clonidine is among the most prescribed medications for youth with insomnia, and may be efficacious

Treating pediatric insomnia

Clinical Point

The effectiveness of exogenous melatonin may be decreased in patients with decreased CYP1A2 activity

in youth with neurodevelopmental disorders and ADHD.[13] In small retrospective studies, clonidine decreased sleep latency and nighttime awakenings in addition to increasing sleep duration.[14] Also, clonidine was well tolerated but associated with daytime somnolence. Guanfacine—a selective alpha-2 agonist—is also commonly prescribed for insomnia in youth, although results of trials have been equivocal.[15] Given the more rapid absorption and shorter Tmax of clonidine relative to guanfacine, the former may be preferred as a soporific.

Melatonin and melatonin agonists. The primary regulator of the sleep-wake cycle is melatonin, an endogenous hormone produced by the pineal gland in response to changes in retinal light perception. Exogenous melatonin supplementation may be the preferred initial pharmacotherapy for sleep-onset insomnia due to its chronobiotic properties.[16] In clinical studies, both immediate-release[17,18] and extended-release[19] melatonin reduced sleep-onset latency and increased total sleep duration in pediatric patients, although the increase in total duration of sleep was greater with extended-release preparations. Additionally, tolerability data for melatonin in pediatric patients are encouraging. A 2-year randomized trial of prolonged-release melatonin for insomnia in pediatric patients found no adverse effects with regard to growth, body mass index, or pubertal development.[20] Additionally, significant improvements in sleep quality, sleep patterns, and caregiver satisfaction were maintained throughout the trial, and no withdrawal symptoms were observed upon discontinuation.

Melatonin may have a particularly important role in circadian rhythm sleep disorders. In this regard, low-dose melatonin (0.5 mg), when timed relative to the endogenous dim light melatonin onset (DLMO), is more effective in shifting sleep phase than higher doses, which suggests that timing may have greater impact than dosage.[21] Data regarding melatonin administration with respect to DLMO suggest that the optimal administration time is 4 to 6 hours before a child's preferred bedtime, and doses of 0.5 to 1 mg have been effective when given in this window.[22] Variation across studies has contributed to a lack of consensus regarding pediatric melatonin dosing. For example, .05 mg/kg may be a minimal effective dose when given 1 to 2 hours before bedtime[18]; however, in surveys doses vary considerably, with typical doses of 2.5 to 3 mg for prepubertal children and 5 mg for adolescents.[5] Of note, in patients with decreased cytochrome P450 (CYP) 1A2 activity, lack of diurnal variation in melatonin serum concentration may decrease the effectiveness of melatonin.[16]

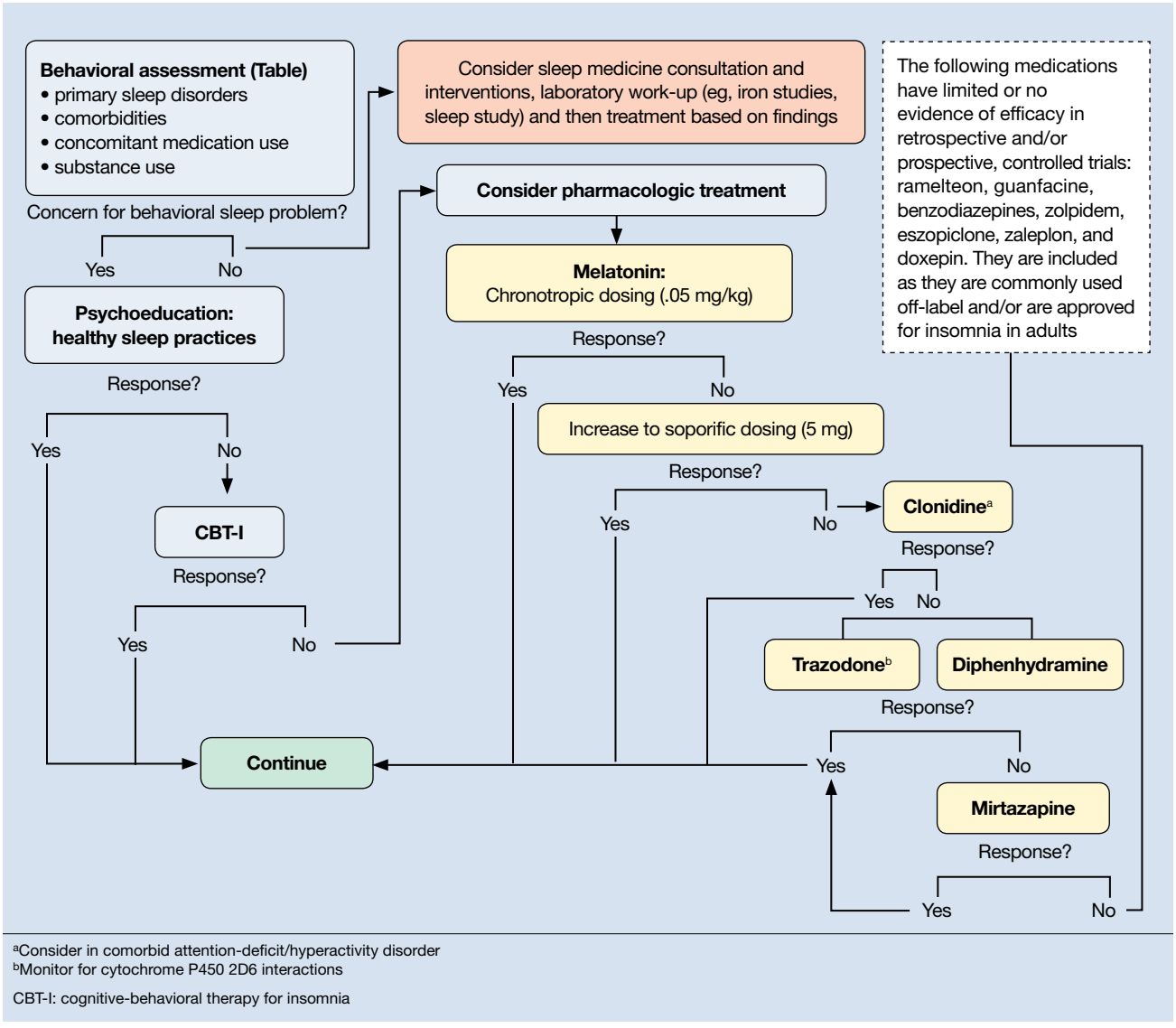
Ramelteon is a potent agonist of the melatonin MT1 and MT2 receptors, with a significantly higher binding affinity than melatonin in vitro. In case reports, ramelteon was well-tolerated, improved delayed sleep onset, and decreased nighttime awakenings.[23]

Zolpidem, eszopiclone and zaleplon. Studies of selective GABAergic modulators and benzodiazepines have not produced positive results in prospective trials of youth with insomnia. Zolpidem was studied in children and adolescents (N = 201) with ADHD; although sleep latency did not differ between zolpidem and placebo, some significant improvements were observed in adolescents.[24] Zolpidem was generally well tolerated, with approximately 10% of youth discontinuing due to adverse effects. Additionally, eszopiclone—which has a longer duration of action compared with zolpidem—has been studied in children and adolescents with ADHD (N = 486) who were also evaluated with a sleep study. No differences were observed between placebo and eszopiclone in terms of sleep latency and approximately 10% of patients discontinued treatment as a result of adverse events.[25] We were unable to locate any prospective trials of zaleplon or benzodiazepine receptor agonists for insomnia in youth, although some reports suggest that clonazepam may have a possible role for specific parasomnias.[26,27]

Dual orexin receptor antagonists. Suvorexant, an antagonist of the wakefulness-promoting neuropeptide orexin, improved subjective sleep quality in a prospective trial of adolescents with insomnia (N = 30), although dropout was high (44%).[28] Of those patients, reasons for discontinuation

Figure

Psychotherapeutic and pharmacologic treatment of pediatric insomnia



[a]Consider in comorbid attention-deficit/hyperactivity disorder
[b]Monitor for cytochrome P450 2D6 interactions

CBT-I: cognitive-behavioral therapy for insomnia

included loss to follow-up, lack of effectiveness, and abnormal dreams. We were unable to locate any trials of lemborexant in pediatric patients.

Atypical antidepressants. Trazodone is commonly prescribed for insomnia in pediatric patients with comorbid mood or anxiety disorders. In open-label studies of children and toddlers, trazodone may be well-tolerated and improve sleep.[29] Additionally, development of a physiologically based pharmacokinetic model to inform trazodone dosing for youth with insomnia is underway.[30] Some studies in adolescents with depression suggest that caution should be used when combining trazodone with medications that inhibit CYP2D6. In the Treatment of SSRI-Resistant Depression in Adolescents study, none of the patients who were treated with trazodone (vs other soporifics) improved.[31] This may relate to CYP2D6 interactions and accumulation of methyl-chloro-piperazine (mCPP), a trazodone metabolite that is associated with dysphoria, irritability, and depression.[31] This finding has been replicated in a separate cohort of depressed adolescents.[32]

Because of its antihistaminergic effects, mirtazapine has been used to treat insomnia in adults. One open-label study of

Clinical Point

Consider whether insomnia is the child's primary disorder, or is secondary to another diagnosis

mirtazapine in children and young adults ages 3 to 23 with neurodevelopmental disorders suggested that mirtazapine improved behavioral symptoms and insomnia, and was associated with few treatment-limiting adverse effects.[33]

Tricyclic antidepressants. In a retrospective study of youth with insomnia who failed behavioral interventions and melatonin (N = 29), doxepin, a potent H1 antagonist, improved subjective sleep in one-half of patients.[34]

Consultation with pediatric sleep medicine specialists

It often will behoove the psychiatric clinician to review their concerns with a behavioral sleep medicine specialist or a psychologist with specific expertise in the psychotherapeutic treatment of sleep who can provide important guidance regarding the key aspects of treatment. When discussing a particular patient's presentation with the pediatric behavioral sleep psychologist/specialist, consider the following questions:

- Is the child's sleep disorder the primary problem, or is the child's insomnia secondary to another diagnosis (psychiatric or nonpsychiatric)?
- What are the primary sleep-related problems the child/family presents with? How long have the symptoms been present?
- Is the sleep disorder interfering with the child's functioning, either academically or socially? Does the child's sleep problem interfere with other family members' sleep?
- Does the child have a comorbid psychological conditions such as ADHD, depression, or anxiety, and/or is undergoing treatment for these disorders, which may play a role in the sleep problem?
- Is a sleep study warranted?

A sleep study, also known as polysomnography (PSG), is a diagnostic test in which physiologic parameters are continuously recorded during a period of sleep via electroencephalography, electromyography, electrooculogram, electrocardiogram, airflow sensors, pulse oximeter, body position monitors, and video. In 2012, the American Academy of Sleep Medicine published evidenced-based practice parameters for respiratory and nonrespiratory indications for PSG.[35] It is most commonly indicated to rule out obstructive sleep apnea in pediatric patients who exhibit snoring, gasping, irregular breathing, witnessed apneic events, unusual head positioning, or other signs of obstructive breathing during sleep. Nonrespiratory indications for PSG include children suspected of having periodic limb movement disorder and suspected narcolepsy. Children with frequent parasomnias, epilepsy, or nocturnal enuresis should be clinically screened for presence of comorbid sleep disorders, and PSG would be indicated if there are concerns about a possible sleep-disordered breathing disorder. PSG is also recommended for children with hypersomnia, to differentiate a parasomnia from sleep-related epilepsy, and for children suspected of having restless leg syndrome.[36] PSG is not typically indicated in the initial evaluation of insomnia (unless there is evidence of a comorbid sleep disorder), circadian rhythm disorders (ie, delayed sleep phase syndrome), or for evaluation of children with sleep-related bruxism.[3] Special considerations for PSG in children include ensuring a parent or guardian is always with the child, providing developmentally appropriate sleeping arrangements, arranging family tours of the sleep lab prior to the study, and accommodating for earlier bedtimes.[37]

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Related Resource

- Hamill Skoch S, Stimpfl JN, Strawn JR. Pediatric insomnia: Assessment and diagnosis. Current Psychiatry. 2021;20(12):9-13,24-25. doi: 10.12788/cp.0194

Drug Brand Names

Clonidine • Catapres
Clonazepam • Klonopin
Doxepin • Silenor
Eszopiclone • Lunesta
Guanfacine • Intuniv, Tenex
Hydroxyzine • Vistaril
Lemborexant • Dayvigo
Mirtazapine • Remeron
Ramelteon • Rozerem
Suvorexant • Belsomra
Trazodone • Oleptro
Zaleplon • Sonata
Zolpidem • Ambien

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Bottom Line

Techniques to promote healthy sleep in pediatric patients include behavioral interventions such as setting a developmentally appropriate bedtime and a consistent wake time, establishing bedtime routines, and encouraging relaxation/wind-down period before bed. Cognitive-behavioral therapy for insomnia (CBT-I) may include cognitive restructuring of anxious thoughts, relaxation training, stimulus control, and sleep restriction. Use of medications may be indicated for children and teens who have not responded to CBT-I or soporific dosing of melatonin.

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Clinical Point

Polysomnography is most commonly indicated to rule out obstructive sleep apnea